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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,924	09/12/2003	Paul P. Latta	LATTA.002A	7335

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EXAMINER
BELYAVSKYI, MICHAIL A

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,924	LATTA, PAUL P.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The **examiner** of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michail Belyavskyi, Group Art Unit 1644, Technology Center 1600

Claims 2-9 are pending

2. Applicant's election of primary cell species ,allogenic cells species and without immunosuppression in the reply filed on 10/12/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 2-9 are under consideration in the instant application.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

4. Applicant notes that an IDS was submitted with the prior application 09/226742. However these citations have been crossed out as said references cited in said parent application cannot be found. Applicant is invited to resubmit such references to complete the instant file. The examiner apologizes for any inconvenience to applicant for having to resubmit such documents.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" A method of preventing onset of Type I diabetes in a mammal" claimed in claim 2 represent a departure from the specification and the claims as originally filed. The passages pointed by the applicant do not provide a clear support for the "A method of preventing onset of Type I diabetes in a mammal". The specification and the claims as originally field only support " A method of preventing diseases".

7. Also an issue that Claims 2-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide **enablement** for a method of preventing onset of Type I diabetes in a mammal , comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses the effects of the implanting of insulin-producing cells on the level of blood glucose using streptozotocin-induced diabeties in murine experimental model. (See Examples 1-2 in particular). Examples 3-7 in the instant Specification are prophetic examples that indicate what the inventor thinks might happen in the experiments which have not actually been performed. The specification does not adequately teach how to effectively prevent onset of type I diabetes in mammal predisposed to type I diabetes , comprising implanting insulin-producing cells encapsulated in a biologically-compatible membrane. Mestas et al (J. of Immunology, 2004, 172, pages 2731-238) teach that there exist significant differences between mice and humans in immune system development, activating and response to challenge in both the innate and adaptive arms. As therapies for human diseases become ever more sophisticated and specifically targeted it becomes increasing important to understand the potential limitations

of extrapolating data from mice to humans. The literature is littered with the examples of therapies that work well in mice but fail to provide similar efficacy in humans. Teuveson et al., (Immun. Review 1993, N136, pages 101-107) teach that one problem with rodent models of transplantation is that rejection is easily overcome in said models in comparison to the difficulty of overcoming allograft rejection in human (see page 100 in particular). Teuveson et al., further teach that " however today's small animal models seem to be insufficient to produce data for clinical decision-making" and further raises doubt as to whether large animal models can be applied to clinical situations, due to species-specific reactions to treatment (see page 101 in particular). Feldman et al (Transplant. Proc. 1998, 30, 4126-4127) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously in vitro but a fairly high portion of them still fail *in vivo*. Moreover, since the method of treating and preventing onset of type I diabetes in mammal predisposed to type I diabetes , comprising implanting insulin-producing cells encapsulated in a biologically-compatible membrane can be species- and model-dependent (see Van Noort et al. International Review of Cytology, 1998, v.178, pages 127-204, Table III in particular) , it is not clear that reliance on the *in vivo* murine data accurately reflects the relative any mammal and human efficacy of the claimed therapeutic strategy. Van Noort et al., further indicate factors that effect immune response such as genetic, environmental and hormonal (Page 176, Paragraph 3). The ability of a host to enhance an immune response will vary depending upon factors such as the condition of the host and burden of disease.

Thus, as has been discussed supra, the state of the art is that it is unpredictable form the *in vivo* murine data disclosed in the specification as whether the instant invention can be used for the *in vivo* treatment of diabetes in any mammals including human. Therefore, it is not clear that the skilled artisan could predict the efficacy of a method of preventing onset of type I diabetes in mammal predisposed to type I diabetes , comprising implanting insulin-producing cells encapsulated in a biologically-compatible membrane. Thus in the absence of working examples or detailed guidance in the specification, the intended uses of the claimed method of preventing onset of Type I diabetes in any mammal, including human are fraught with uncertainties.

Further, the burden of enabling the prevention of a disease (i. e. the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those humans susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. Further, the specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to Type I diabetes within the scope of the presently claimed invention. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed compounds

in preventing these disease states. Knip M (Acta Pediatr. Suppl., 1998, V.452, pages 54-62) teaches that currently the state of the art is that successful prevention of type I diabetes has at least two precondition. First, one must be able to identify individuals at increase risk for progression to type I diabetes and second, must have an intervention modality with less severe adverse effects than those associated with disease itself. Total eradication of clinical type I diabetes cannot be expected in the next century, as it is probable that a combination of different interventions will be needed to achieve an optimal effect (see entire document, page 60 in particular). Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of preventing onset of type I diabetes in mammal predisposed to type I diabetes , comprising implanting insulin-producing cells encapsulated in a biologically-compatible membrane in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

9. Claims 2-5, 7-9 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,703,017 or by US Patent 5,425764.

US Patent '017 teaches a method of treating and preventing onset of type I diabetes in a mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract and columns 6, 8, 9 –14 and Example 12 in particular) . US Patent '017 teaches that insulin producing cells are pancreatic islet cells from primary cell source (see columns 8 and 11 in particular). US Patent '017 teaches that pancreatic islet cells are from the same species as the mammal and are implanted interperitoneally into the tissue of a mammal beneath the kidney capsule (see overlapping columns 13-14 and Example 2 in particular). US Patent '017 teaches that encapsulation of said insulin-producing cells in biologically compatible membrane for success of implantation is well known in the art (see column 12 and Example 12 in particular).

US Patent '764 teaches a method of treating and preventing onset of diabetes in a mammal comprising implanting insulin-producing cells encapsulated in a biologically compatible membrane (see entire document, Abstract and overlapping columns 5-6 in particular). US Patent '764 teaches that insulin producing cells are pancreatic islet cells (see column 1 and 4 in particular). US Patent '764 teaches that cells are implanted interperitoneally (see column 5 in particular).

The references teaching anticipates the claimed invention.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 2-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,703,017 or by US Patent 5,425764 each and in view of US Patent 5,529,914.

The teaching of US Patent 6,703,017 and US Patent 5,425764 have been discussed, supra.

US Patent 6,703,017 or US Patent 5,425764 does not explicitly teaches that a method of preventing onset of Type I diabetes wherein insulin-producing cells are encapsulated in a conformal coating comprises polyethylene glycol (PEG).

US Patent '914 teaches a new type of biocompatible membrane as a covering to encapsulate biological materials, comprising PEG that is acceptable for implants in mammalian. (see entire document, Abstract in particular). US Patent '914 teaches that various types of cells can be encapsulated in said biocompatible membrane and that said encapsulation will prevent rejection of encapsulated cells during transplantation (see column 10 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '914 to those of US Patent ' 017 or US Patent '764 to obtain a claimed method of preventing onset of Type I diabetes wherein insulin-producing cells are encapsulated in a conformal coating comprises polyethylene glycol (PEG).

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because encapsulation of cells in biologically compatible membrane comprising PEG will prevent rejection of encapsulated cells during transplantation as taught by US Patent '914. Said type of biocompatible membrane can be used to substitute the different type of biocompatible membrane for successful implantation of insulin-producing cells in the method of treating or preventing Type I diabetes taught by US Patent ' 017 or US Patent '764. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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December 10, 2004

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